

Incorporating Water in Small-Angle Scattering Calculations of Proteins

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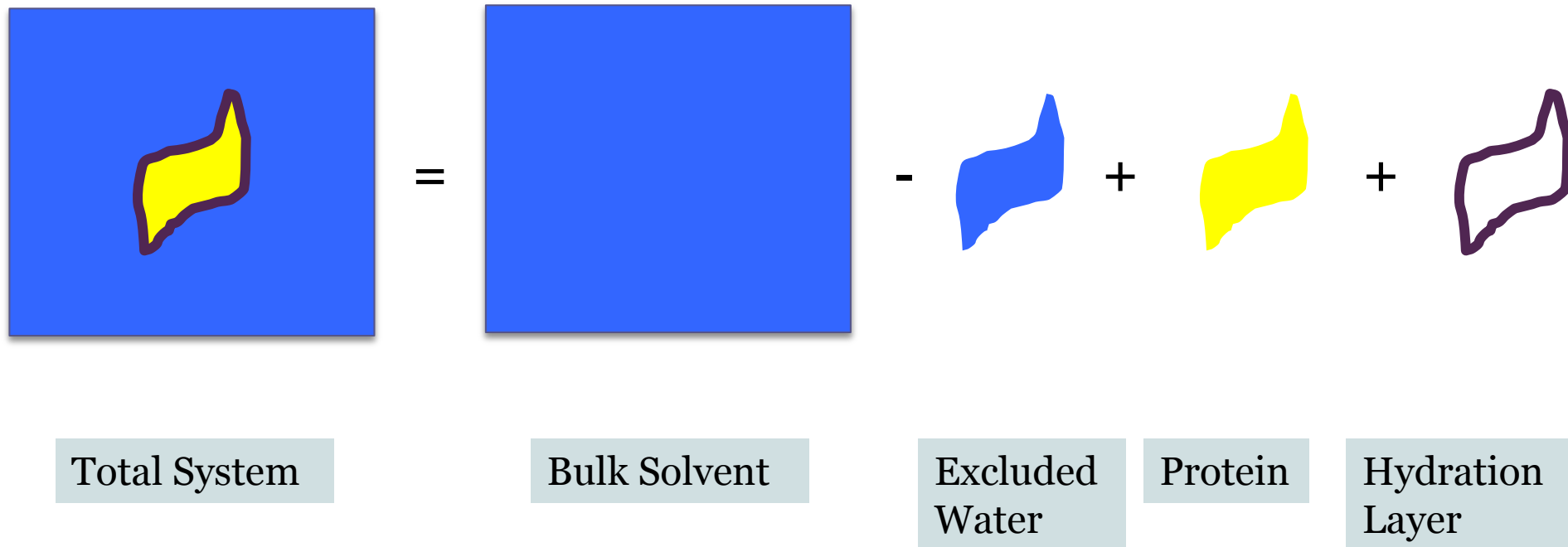
Dr. Joseph Curtis



Outline

- Background
 - Proteins
 - Small-Angle X-ray and Neutron Scattering
 - Molecular Dynamics Simulations
- Simulation Analysis
 - Atomic Fluctuations and Orientations
 - X-ray vs. Neutron Scattering Data

Proteins in Solution

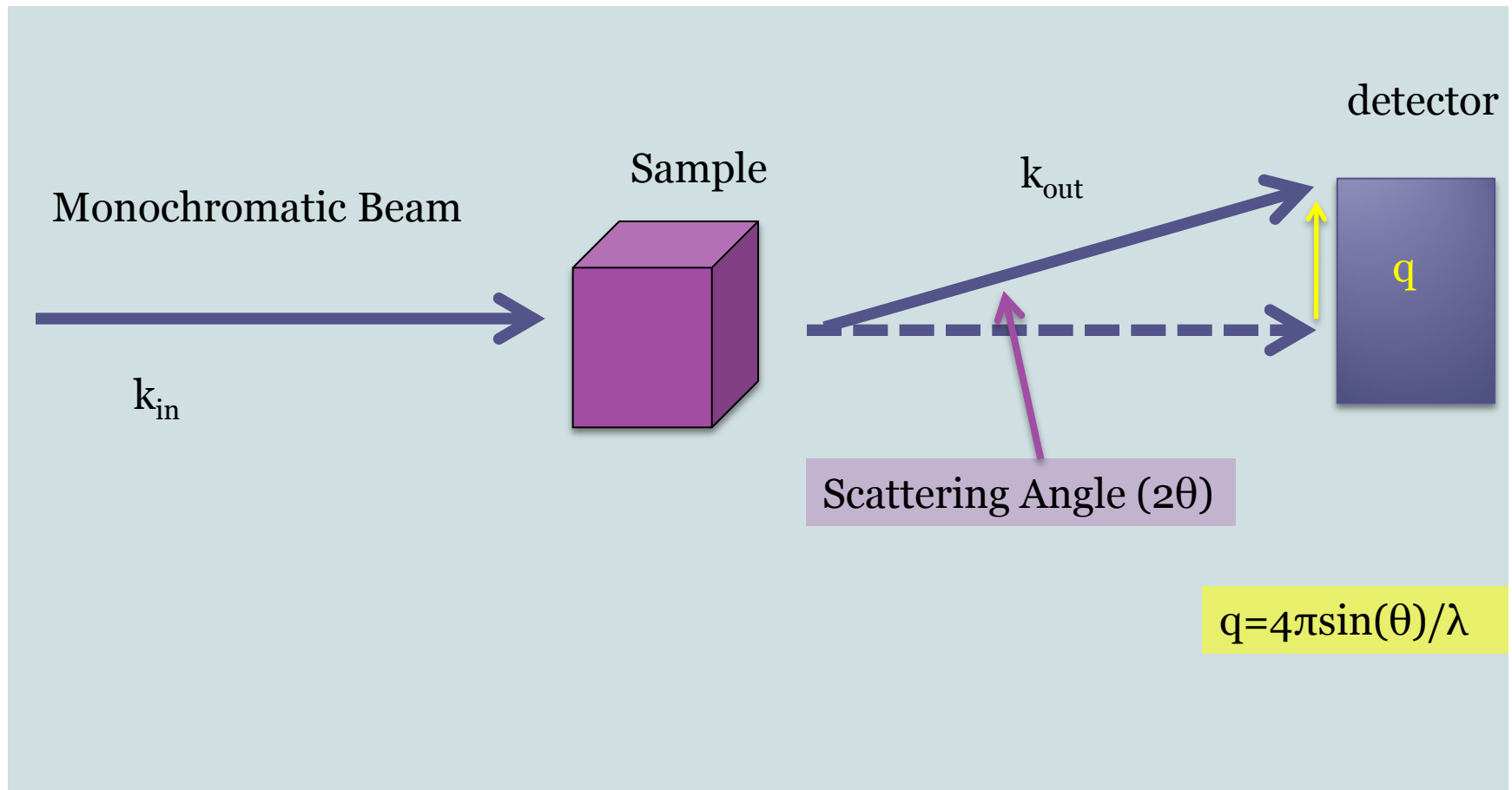


Biological Sciences-Biophysics

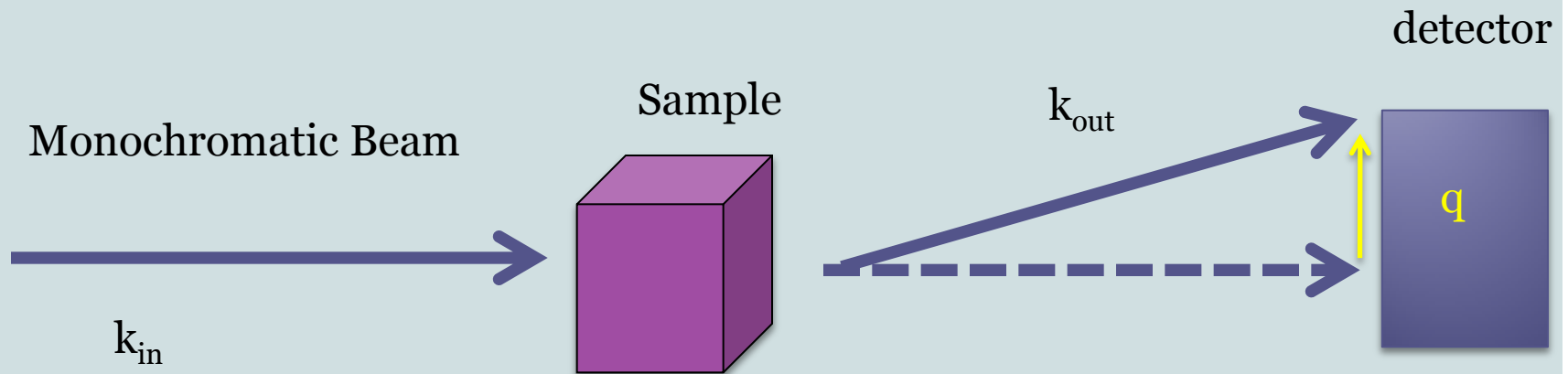
D. I. Svergun, S. Richard, M. H. J. Koch, Z. Sayers, S. Kuprin, and G Zaccai

Protein hydration in solution: Experimental observation by x-ray and neutron scattering

Small-Angle Scattering



Scattering Basics



Amplitude

$$A(q) = \sum_j^N b_j e^{-i\mathbf{q} \cdot \mathbf{r}_j}$$

Scattering Intensity

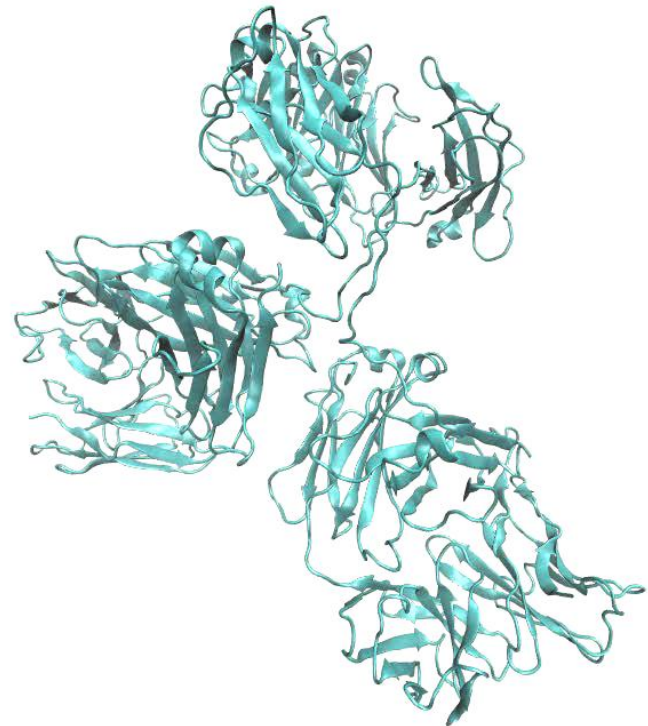
$$I(q) = |A(q)|^2$$

\mathbf{r}_j = position of atom j
 b_j = position of atom j
 N = number of atoms

$$\mathbf{q} = \mathbf{k}_{out} - \mathbf{k}_{in}$$

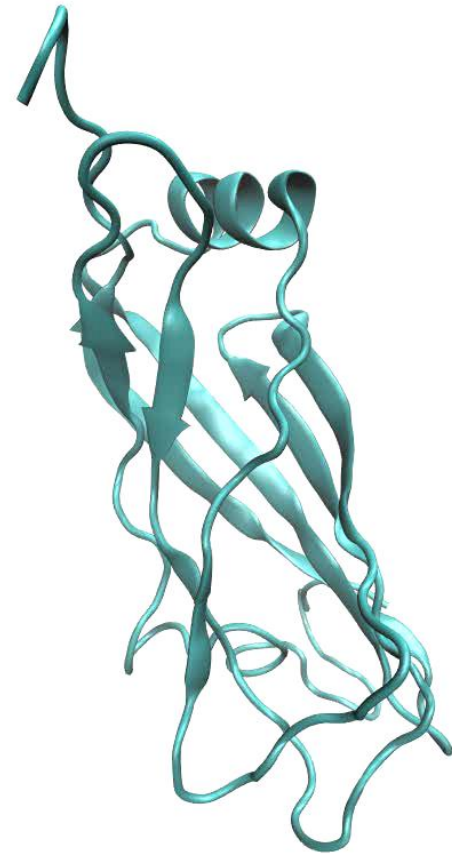
Molecular Dynamics Simulations

- Simulation technique used for computing the properties of a molecular system over time.
- Molecular dynamics (MD) simulations are powerful tools for modeling protein interactions with the solvent.
- Used to calculate dynamic and complex biological systems.



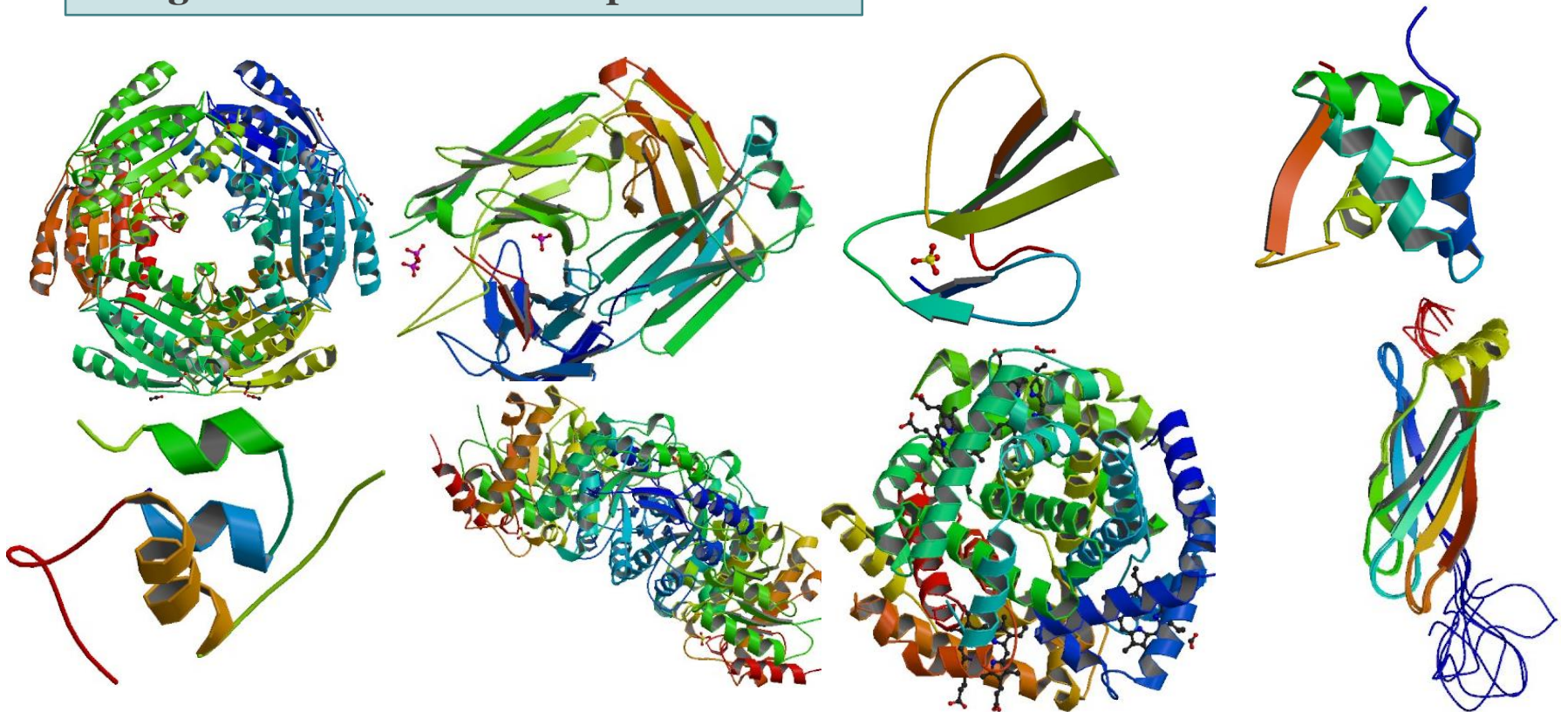
Using Molecular Dynamics

- Took a snapshot for every frame in the simulation trajectory.
 - Snapshot every 100 ps
 - Total trajectory length is 2 ns
- Used different snapshots to determine the effect of atomic fluctuations on scattering data



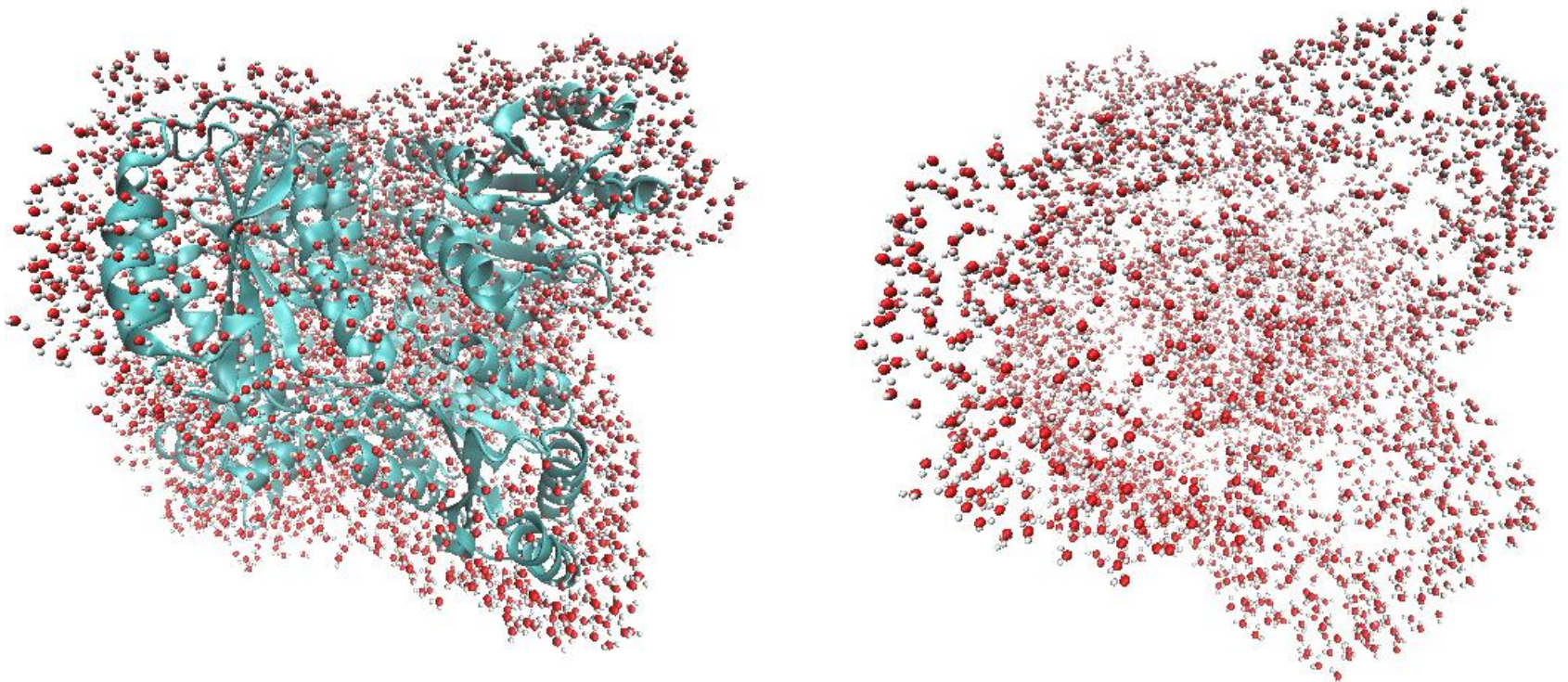
Using Molecular Dynamics

Set up molecular dynamics simulations
using NAMD for 18 different proteins



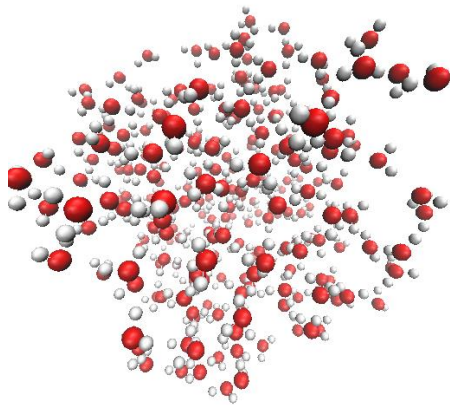
Hydration Layer

Waters that interact with the protein surface



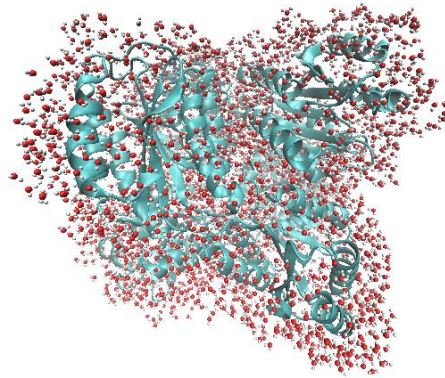
Excluded Water

Water displaced
by the protein



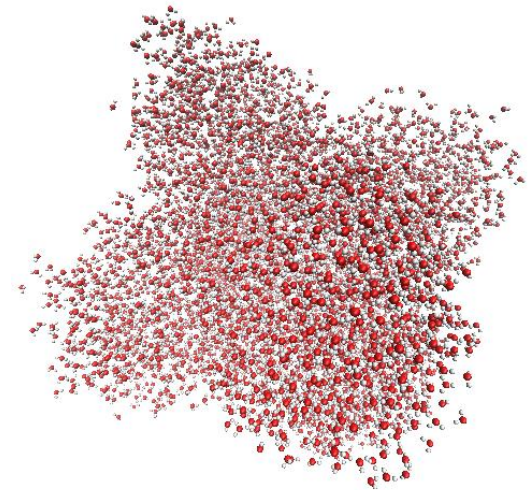
Water Box

+



Protein and
Hydration
Layer

→

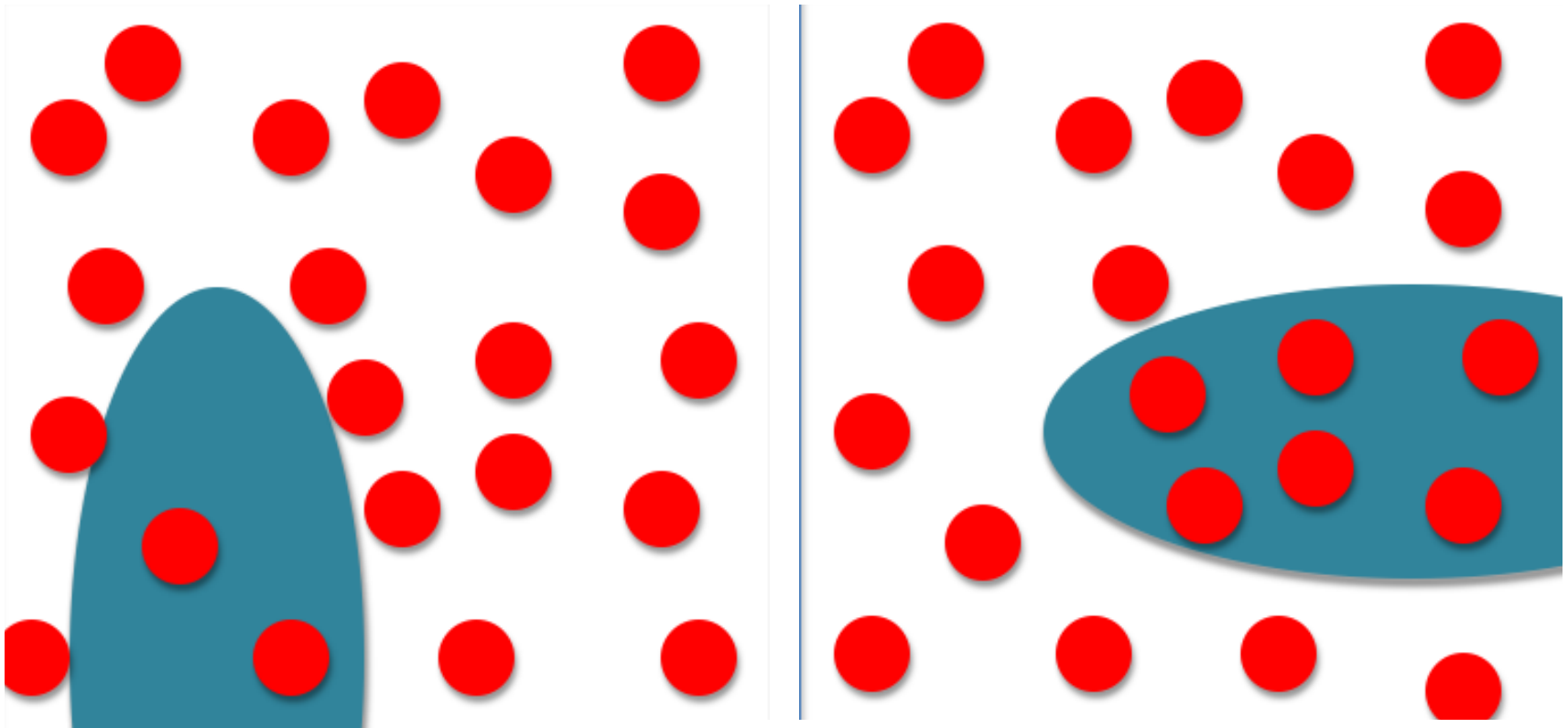


Excluded Waters

Calculating Scattering Data

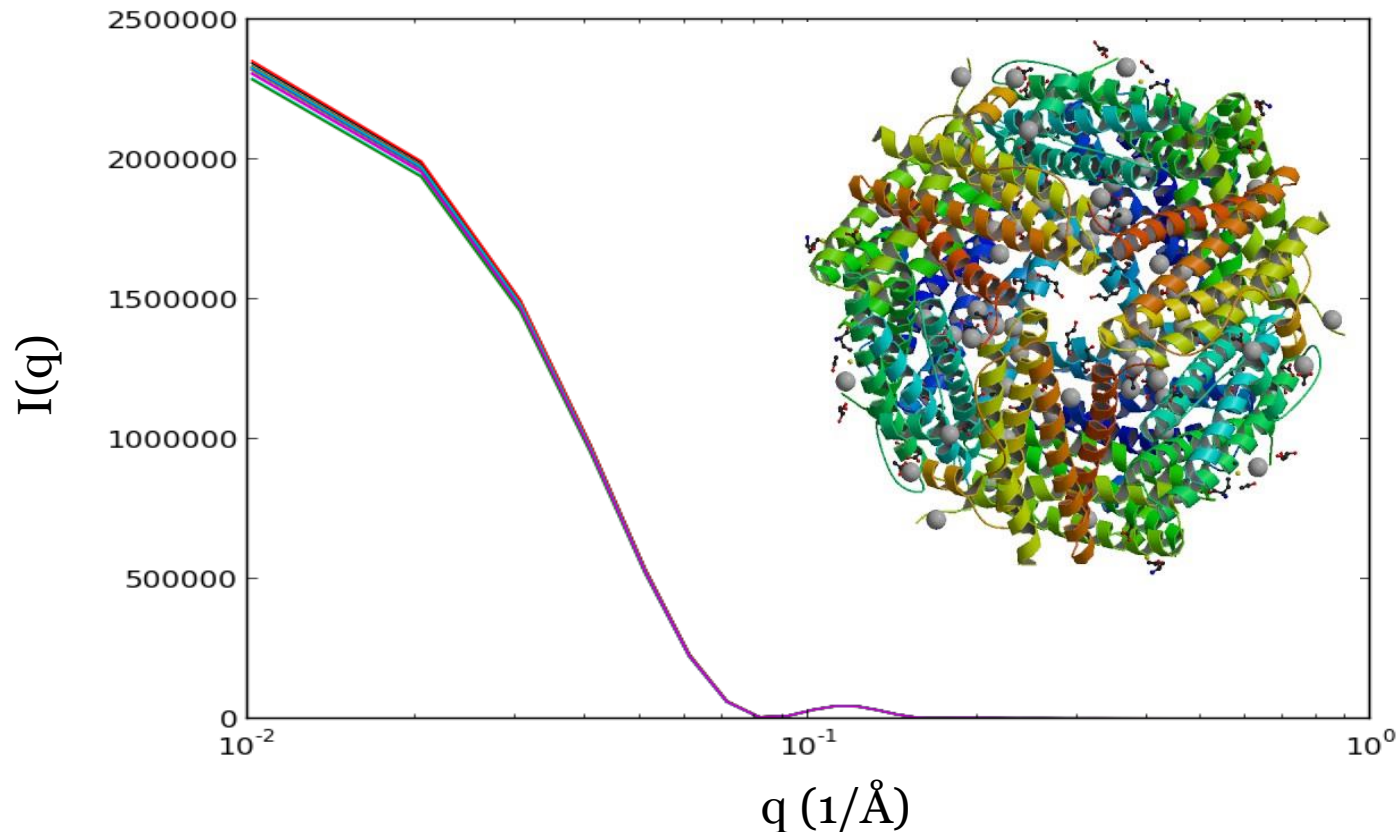
- Used a program called SASSIE to calculate small-angle x-ray and neutron scattering data for each protein, its hydration layer, and the excluded waters

The Effect of Orientation on Small-Angle Scattering Data



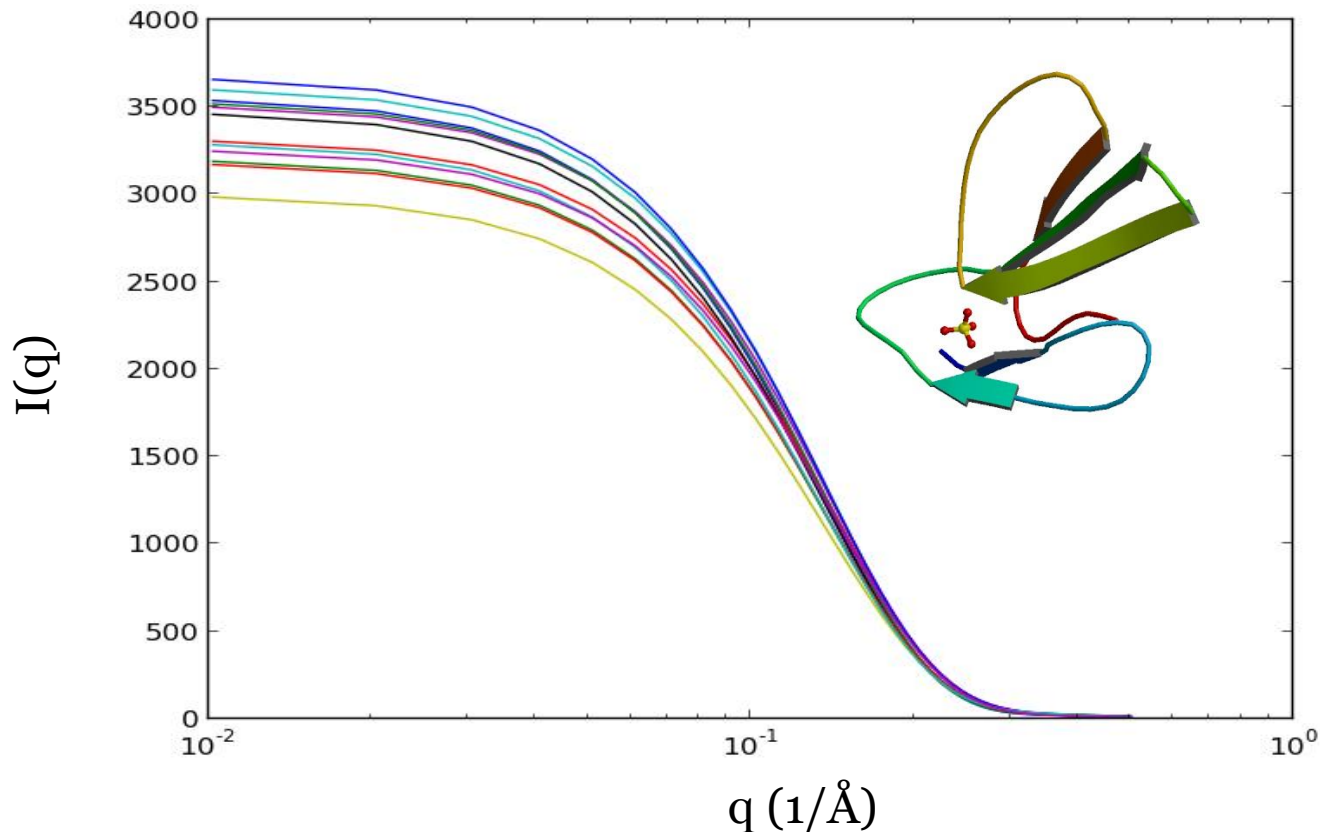
The Effect of Orientation on Small-Angle Scattering Data

Bacterioferritin Excluded Waters

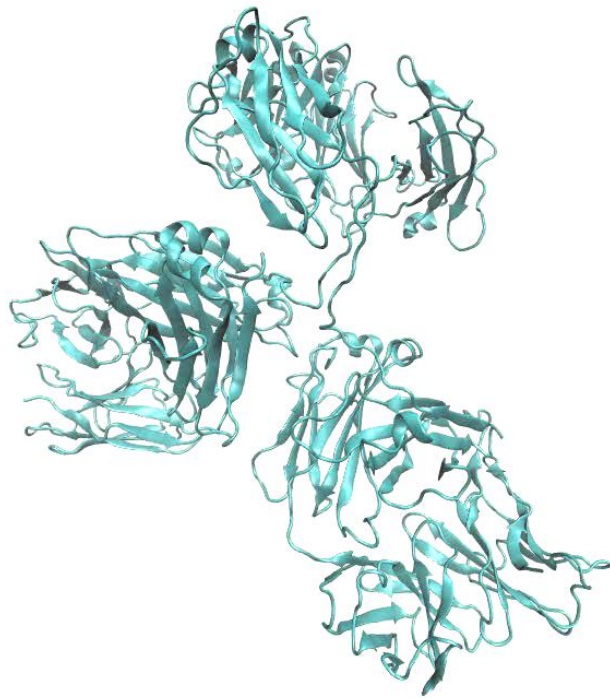


The Effect of Orientation on Small-Angle Scattering Data

Erabutoxin Excluded Waters

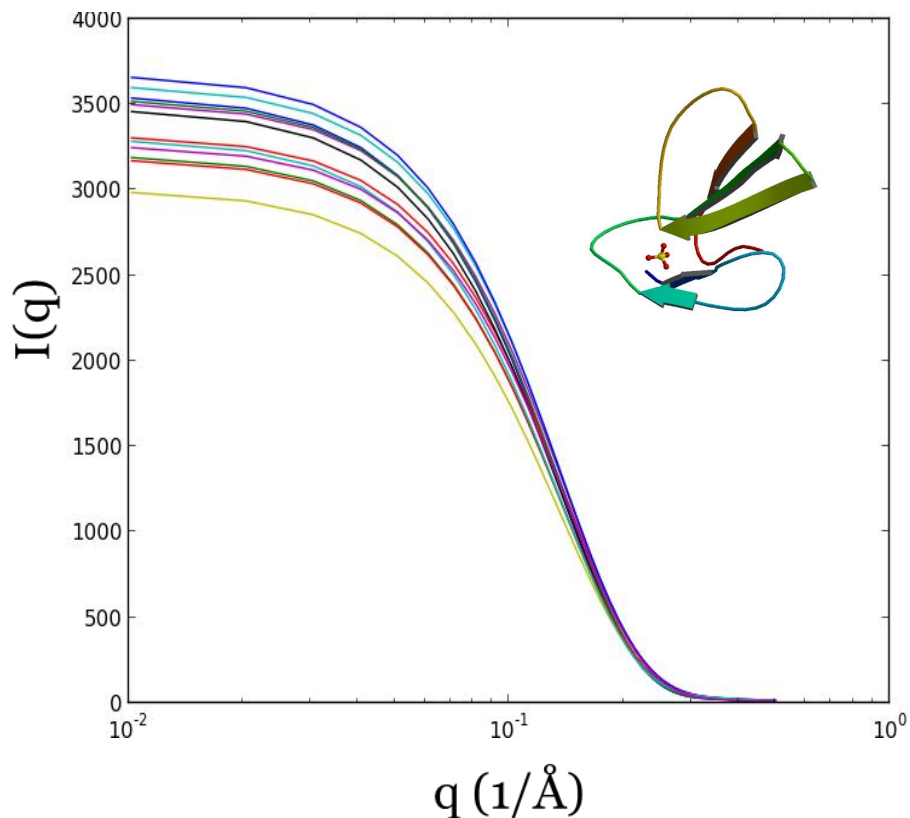


The Effect of Atomic Fluctuations on Small-Angle Scattering Data

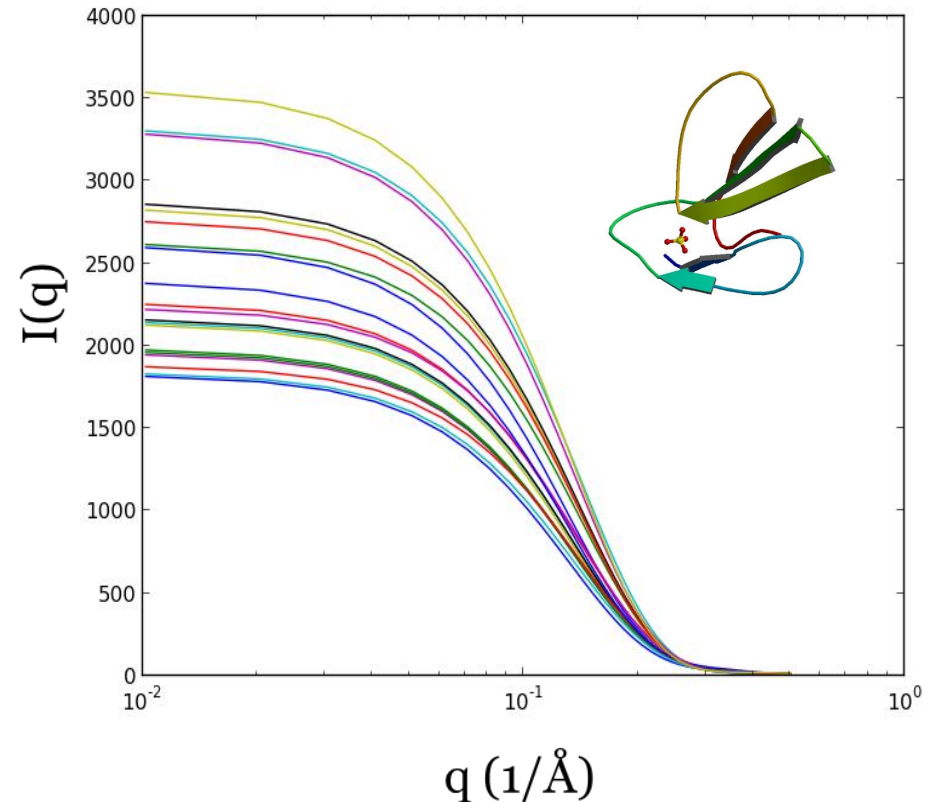


The Effect of Atomic Fluctuations: Erabutoxin

Changes in orientation

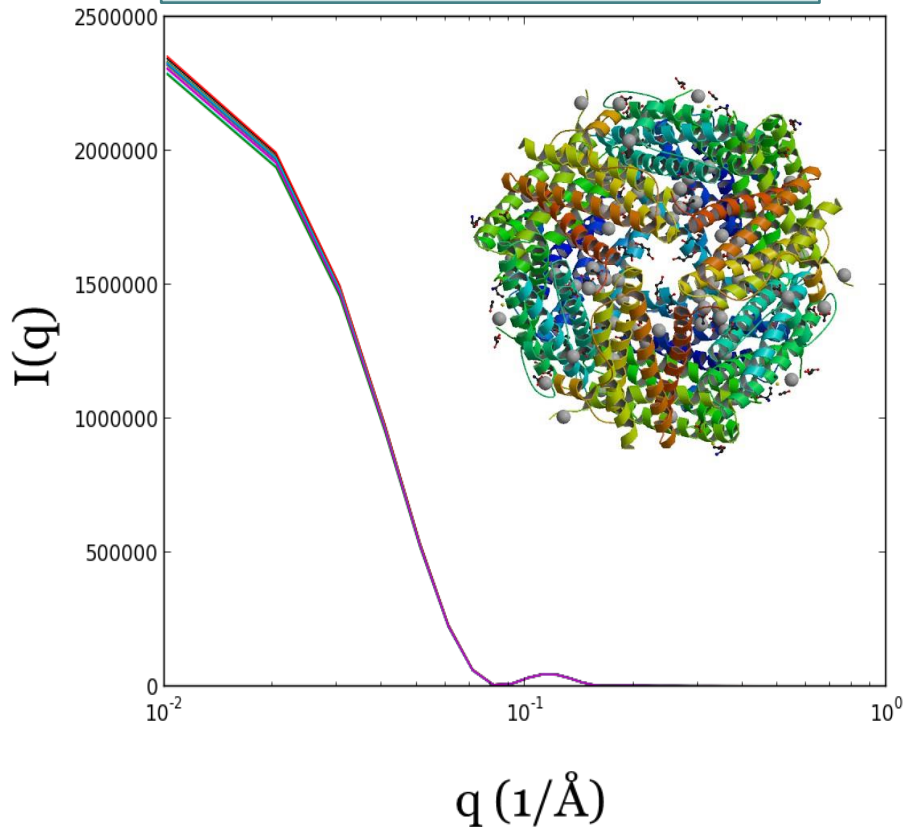


Changes in frame

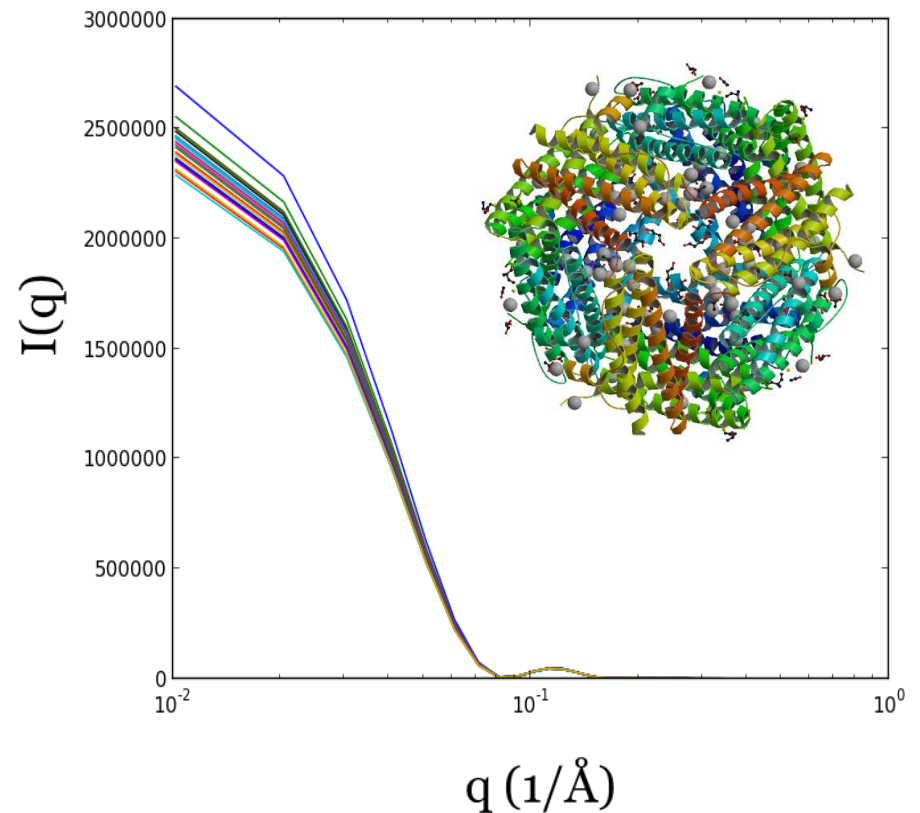


The Effect of Atomic Fluctuations: Bacterioferritin

Changes in orientation

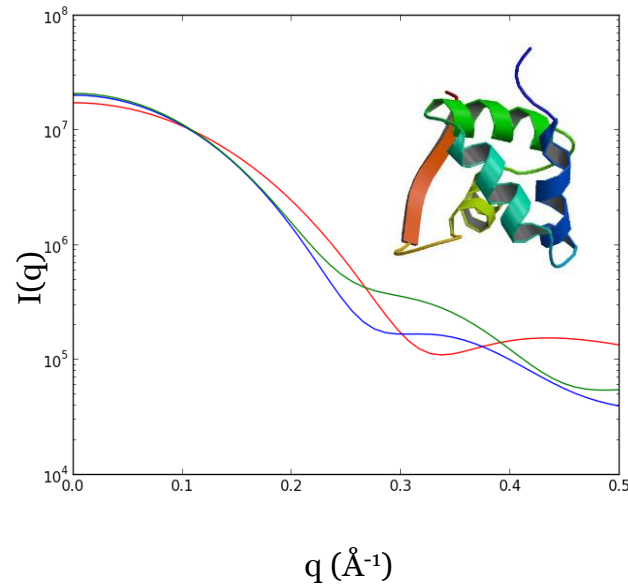


Changes in frame

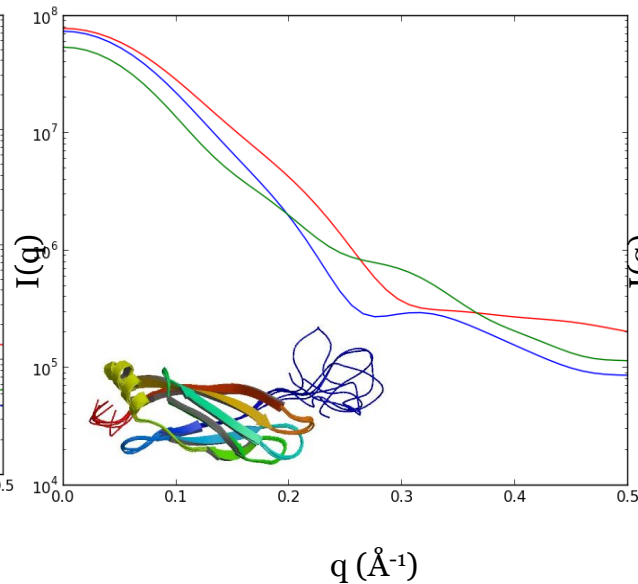


Average Small-Angle X-ray Scattering Data

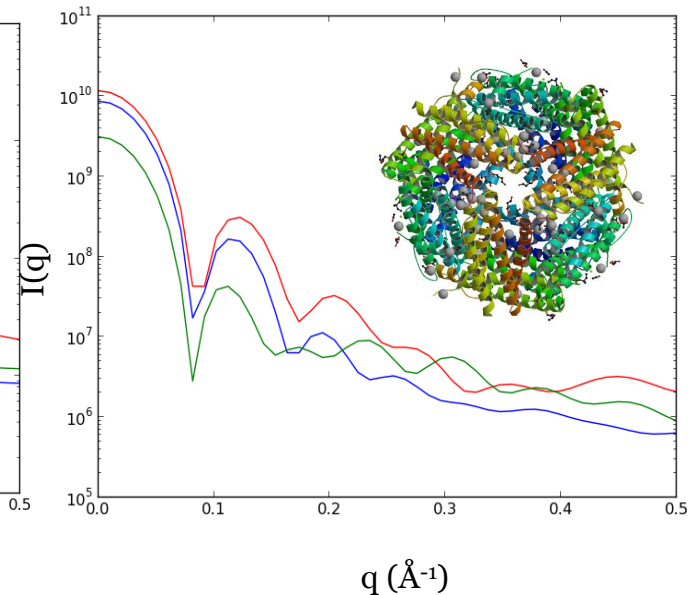
Protein
Excluded Waters
Hydration Layer



1HYP: Hydrophobic



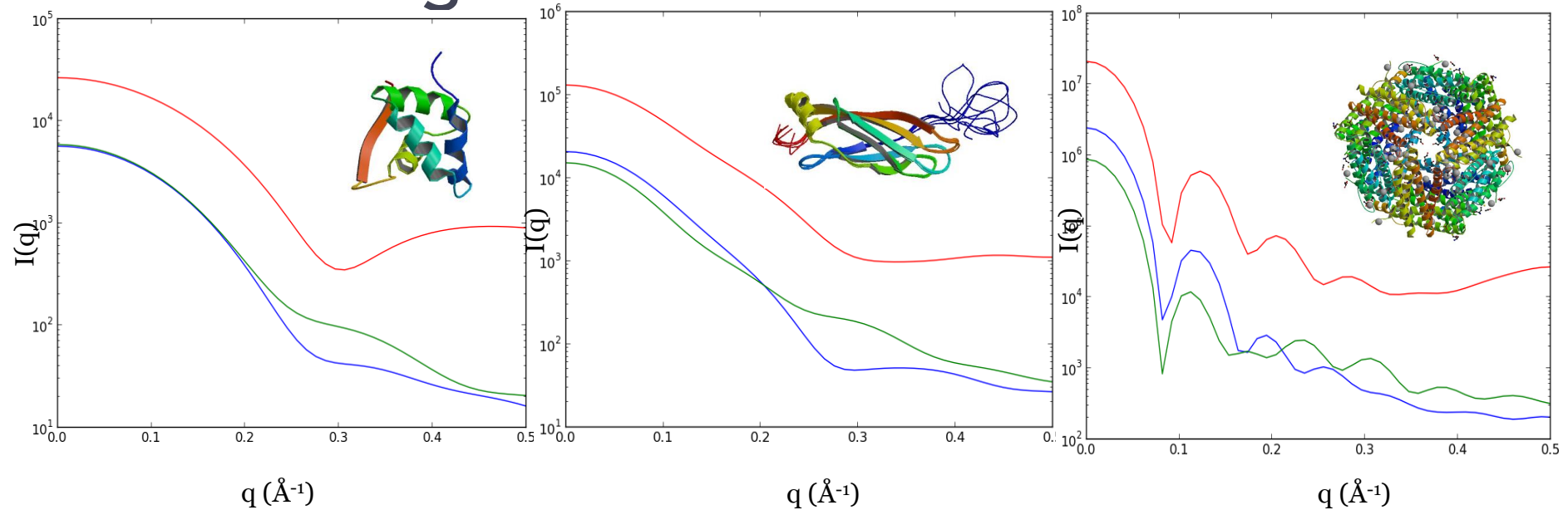
1XO8: Hydrophilic



Bacterioferritin: Largest

Average Small-Angle Neutron Scattering Data

Protein
Excluded Waters
Hydration Layer



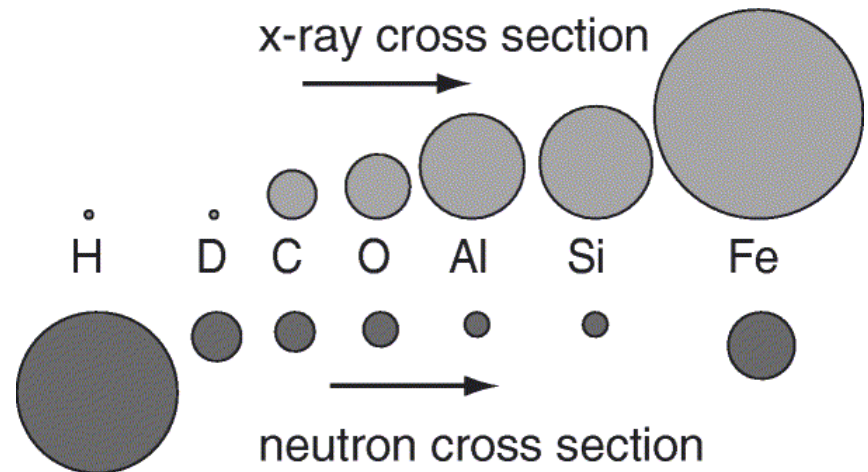
1HYP: Hydrophobic

1XO8: Hydrophilic

Bacterioferritin: Largest

The Effect of Water on Scattering Data

- The solvent is more important in X-ray scattering than in neutron scattering because oxygen plays a stronger role due to its atomic mass.



Conclusion

- Variability of scattering curves is dominated by the movements of the atoms in the protein trajectories.
- At distances greater than 30\AA , the scattering is dominated by the protein itself for X-ray scattering.
- The solvent has a smaller effect on neutron scattering.

Acknowledgments

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